

EDITORIAL COMMENT†

DELETERIOUS EFFECTS OF "BACTERIOPHAGE" THERAPY

Immunologists are familiar with the phenomenon of test-tube synergism between bacteria and homologous bacteriophage, the formation of a 'phage-bacterium complex of exalted pathogenicity and aggressive physiological function. Many investigators have feared that similar conjugations might take place in the animal body, which, under certain conditions, would contraindicate homologous 'phage therapy. Doctors Bronfenbrenner and Sulkin,¹ of Washington University Medical School, therefore, have rendered a valuable service to clinical research by devising a simple experimental method by means of which this fear may be tested.

In their technique, rabbits were injected intracutaneously with an arbitrary dose of low-virulent staphylococci. The rate of development and duration of the resulting local skin lesion were recorded daily in untreated and 'phage-treated animals. In their untreated controls, the local skin lesion reached its maximum size (2.5 square centimeters) by the end of twenty-four hours, and decreased to about half this size by the end of four days, and to about a quarter of the maximum by the end of seven days. Spontaneous healing was effected by the twelfth day.

In their hands, the rate of development, maximum size and rate of healing of this local staphylococcus infection were not affected either favorably or unfavorably by the continuous application of compresses moistened with nutrient broth, nor with "bacteriophage" (*i. e.*, filtered staphylococcus 'phage-lysate) prepared from low-virulent staphylococci. "Bacteriophage," prepared for virulent staphylococci, however, markedly accelerated the local spread of the experimental infection, and almost doubled the maximum size of the local lesion. The 'phage-treated lesions continued at about twice the control size for about eight days. Healing was effected by the thirteenth day.

While their demonstration of the complete absence of all beneficial effects of local 'phage therapy are applicable only to cutaneous lesions treated by moist compresses, their demonstration of a synergistic aggressive substance in certain routine 'phage-lysates is presumably of wider clinical application. They liken this synergistic aggressin to the "Reynals Spreading Factor," which can be isolated from certain animal tissues or bacterial cells.

Whether or not it is possible for the staphylo-aggressin to change a relatively unimportant local staphylococcus infection into a fatal septicemia has not yet been tested. The effects of this aggressive factor on chronic local staphylococcus in-

fections, in which 'phage therapy is presumably complicated (or assisted?) by local allergic reactions, also has not yet been studied.

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OBSERVATIONS ON THE TREATMENT OF MENINGOCOCCUS MENINGITIS*

Many methods for the treatment of meningitis have been promulgated in recent years, with variations in the types of serum used, and in the methods of their introduction.

Some advocate giving the serum by alternating lumbar puncture, with cisternal puncture. Some advocate through and through drainage by combining the above-named punctures, and then introducing the serum. Some advocate its use once in twenty-four hours; some in twelve, etc. One clinician uses the newly marketed meningococcus antitoxin, the next one applies manufacturer's serum, the third still another one, and so on.

Many practitioners never see over two or three cases of the disease in a lifetime of practice, and, naturally, when a case presents itself amidst all this confusion, they are more or less at sea for an exact and rational procedure.

Based on several hundred cases over a decade of experience, during which we have constantly sought for better therapy, we are happy to recommend a newer line of procedure that in all types of cases is giving us much the best results we have so far been able to achieve. Having established the diagnosis, by staining with the standardized technique, of the Gram-negative diplococcus within the neutrophils, either from a scratch through one of the macules on the skin, or from the spinal fluid obtained by lumbar puncture, the spinal fluid is drained off and replaced with antiserum by the gravity method, to which is added 5 cubic centimeters of fresh human serum containing complement, obtained by bleeding some Wassermann-negative donor. When the specific serum fails to flow freely and easily, no more is given. Concurrently, meningococcus antitoxin is given intravenously. The latter procedure is not repeated unless the hematogenous form of the disease predominates.

A culture is promptly made from the spinal fluid, and within twenty-four hours it is tested in the laboratory against the various antisera supplied the market by the different manufacturers. Then only that brand is selected for treatment which agglutinates the living organisms in the most dilute titer, and each time it is used, the human complement is added.

The results have been most prompt and gratifying to both physician and patient. One may never predict which serum will be the one most useful, though one brand has been found to be of service far oftener than all the rest. However, where one has not the facilities for culture and agglutination, a practical procedure may be obtained in

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¹ Bronfenbrenner, J., and Sulkin, S. E.: *Proc. Soc. Exper. Biol. and Med.*, 32:1419 (June), 1935.

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